## **WEST Search History**

Hide Items Restore Clear Cancel

DATE: Thursday, July 06, 2006

Hide?	<u>Set</u> Name	Query	<u>Hit</u> Count
	DB=PG	SPB, USPT, DWPI; PLUR=NO; OP=ADJ	
	L19	(113 same antisense) and (@pd<20020210)	27
	L18	117 and (@pd<20020210)	3
	L17	L14 and ((pei or polyethyleneimine) with (encapsul\$ or cation\$ or lipos\$))	52 ·
	L16	L14 and ((pei or polyethyleneimine) with encapsul\$ or cation\$ or lipos\$)	3316
	L15	L14 and (pei or polyethyleneimine)	236
	L14	L13 and antisense	3555
	L13	((HA or NA or PB2 or PB1 or PA or NP or M1 or M2 or NS) with influenz\$)	5657
	L12	((PB2 or PB1 or PA or NP or M1 or M2 or NS) with influenz\$)	1333
	L11	110 and (pei near5 (cation\$ or lipos\$))	4
	L10	L9 and (@pd<20020210)	48
	L9	L8 and influenza .	396
	L8	antisense and pei	1750
	L7	l6 and (pei or polyethyleneimine)	11
	L6	15 and (cation\$ or lipid or (transfect near2 enhanc\$ or lipos\$))	51
	L5	L4 and (sirna or shrna)	58
	L4	L3 and (influenz\$)	415
	L3	L2 and (influenz\$ or flu\$)	1094
	L2	L1 and (@pd<20030210 or @ad<20030210)	1170
	L1	(PTN or NP or influenz\$ or flu\$) and (sirna or rnai or dsrna or shrna)	3855

END OF SEARCH HISTORY

Welcome to STN International! Enter x:x LOGINID:ssspta1635jxs PASSWORD: TERMINAL (ENTER 1, 2, 3, OR ?):2 Welcome to STN International NEWS 1 Web Page URLs for STN Seminar Schedule - N. America "Ask CAS" for self-help around the clock NEWS 2 New STN AnaVist pricing effective March 1, 2006 NEWS 3 FEB 27 NEWS 4 APR 04 STN AnaVist \$500 visualization usage credit offered NEWS 5 MAY 10 CA/CAplus enhanced with 1900-1906 U.S. patent records KOREAPAT updates resume NEWS 6 MAY 11 NEWS 7 MAY 19 Derwent World Patents Index to be reloaded and enhanced IPC 8 Rolled-up Core codes added to CA/CAplus and NEWS 8 MAY 30 USPATFULL/USPAT2 NEWS 9 MAY 30 The F-Term thesaurus is now available in CA/CAplus The first reclassification of IPC codes now complete in NEWS 10 JUN 02 INPADOC TULSA/TULSA2 reloaded and enhanced with new search and NEWS 11 JUN 26 and display fields JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL NEWS 12 NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006. STN Operating Hours Plus Help Desk Availability NEWS HOURS NEWS LOGIN Welcome Banner and News Items For general information regarding STN implementation of IPC 8 NEWS IPC8 X.25 communication option no longer available NEWS X25 Enter NEWS followed by the item number or name to see news on that specific topic. All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties. Due to scheduled maintenance of STN on Sunday, July 9, 2006, some databases may not be available until 04:00 (4:00 AM) Eastern Daylight Time. \* \* \* \* \* \* \* \* \* \* STN Columbus FILE 'HOME' ENTERED AT 13:57:38 ON 06 JUL 2006

SINCE FILE

ENTRY

0.21

TOTAL

0.21

SESSION

FULL ESTIMATED COST

COST IN U.S. DOLLARS

=> FIL MEDLINE BIOSIS CA EMBASE SCISEARCH

FILE 'MEDLINE' ENTERED AT 13:57:46 ON 06 JUL 2006

FILE 'BIOSIS' ENTERED AT 13:57:46 ON 06 JUL 2006 Copyright (c) 2006 The Thomson Corporation

FILE 'CA' ENTERED AT 13:57:46 ON 06 JUL 2006 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'EMBASE' ENTERED AT 13:57:46 ON 06 JUL 2006 Copyright (c) 2006 Elsevier B.V. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 13:57:46 ON 06 JUL 2006 Copyright (c) 2006 The Thomson Corporation

=> s influenz?

L1 226894 INFLUENZ?

=> s sirna or shrna

L2 21064 SIRNA OR SHRNA

=> s 12 and 12

L3 21064 L2 AND L2

=> s l1 and l2

L4 121 L1 AND L2

=> dup rem 14

PROCESSING COMPLETED FOR L4

L5 62 DUP REM L4 (59 DUPLICATES REMOVED)

=> s 15 and py<=py2003

DATE SPECIFICATION IS NOT VALID

Date specifications may use ranges and numeric operators. The date itself can be in any of the following general formats:

STN Format: YYYYMMDD

Slash Format: MM/DD/YYYY or MM/YYYY

Dot Format: DD.MM.YYYY or MM.YYYY

Text Format: February 10, 1987 Feb 1989

Feb. 10, 1987 1990

Feb. 10, 2000 1998 - 2001

Feb 10, 1987 July 1997 - May 2002 10 February 1987 March 5 - 8, 1990 10 Feb 2007 April - June, 1999

Any year entered with only two digits will be interpreted as being in the range 1900-1999. Thus, Mar 12 01 will be searched as 19010312.

=> s 15 and py<=2003 1 FILES SEARCHED...

L6 13 L5 AND PY<=2003

=> s 16 and (11 (p) 12)

L7 6 L6 AND (L1 (P) L2)

=> s 15 and py<=2002 1 FILES SEARCHED...

```
L8
```

```
=> s CHEN, J?/au; EISEN, H?/au; GE, Q?/au
L9 ·
        98287 CHEN, J?/AU
```

EISEN, IS NOT A RECOGNIZED COMMAND COMMAND STACK INTERRUPTED. ENTER "DISPLAY HISTORY" TO SEE WHICH COMMANDS WERE EXECUTED.

The previous command name entered was not recognized by the system. For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> s EISEN, H?/au; s GE, Q?/au 2367 EISEN, H?/AU L10

1110 GE, Q?/AU L11

=> s 19 or 110 or 111 101544 L9 OR L10 OR L11 L12

=> s 112 and (11 or 12) 3 FILES SEARCHED...

397 L12 AND. (L1 OR L2) L13

=> dup rem 113 PROCESSING COMPLETED FOR L13

157 DUP REM L13 (240 DUPLICATES REMOVED) L14

=> s l14 and py<=2003 1 FILES SEARCHED... L15 74 L14 AND PY<=2003

=> s 115 and 11

L16

63 L15 AND L1

=> d his

(FILE 'HOME' ENTERED AT 13:57:38 ON 06 JUL 2006)

FILE 'MEDLINE, BIOSIS, CA, EMBASE, SCISEARCH' ENTERED AT 13:57:46 ON 06 JUL 2006

226894 S INFLUENZ? L1L221064 S SIRNA OR SHRNA 21064 S L2 AND L2 L3

L4121 S L1 AND L2 L5

62 DUP REM L4 (59 DUPLICATES REMOVED)

. L6 13 S L5 AND PY<=2003 6 S L6 AND (L1 (P) L2) L7 L8 5 S L5 AND PY<=2002

L9 98287 S CHEN, J?/AU 2367 S EISEN, H?/AU L10 L11 1110 S GE, Q?/AU

101544 S L9 OR L10 OR L11 L12

L13 397 S L12 AND (L1 OR L2) 157 DUP REM L13 (240 DUPLICATES REMOVED) L14

L15 74 S L14 AND PY<=2003

63 S L15 AND L1 L16

=> s 116 and 12

1 L16 AND L2 L17

=> s l17 or l6 L18 13 L17 OR L6

=> dup rem 118
PROCESSING COMPLETED FOR L18

L19 13 DUP REM L18 (0 DUPLICATES REMOVED)

=> d l19 bib abs 1-13

L19 ANSWER 1 OF 13 CA COPYRIGHT 2006 ACS on STN

AN 144:127482 CA

TI Inhibition of class II antigen invariant chain (Ii) expression in mammalian cells using small interfering RNAs (siRNAs)

IN Xu, Minzhen; Humphreys, Robert

PA USA

SO U.S. Pat. Appl. Publ., 47 pp., Cont.-in-part of U.S. Ser. No. 127,347. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 5

T 1 774 + /	CHI				
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	US 2006008448	A1	20060112	US 2004-999208	20041129
	US 5726020	Α	19980310	US 1996-661627	19960611 <
	US 6368855	B1	20020409	US 1998-205995	19981204 <
	US 2003054365	A1	20030320	US 2002-54387	20020122 <
	US 2003198626	A1	20031023	US 2002-127347	20020422 <
PRAI	US 1996-661627	<b>A</b> 1	19960611		
	US 1998-36746	B2	19980309		
	US 1998-205995	A3	19981204		
	US 2002-54387	B2	20020122	•	
	US 2002-127347	A2	20020422		

The present invention is directed toward compns. and methods involving the AB inhibition of Ii antigen (MHC Class II antigen invariant chain) expression in cells for the purpose of altering antigen presentation pathways. More specifically, disclosed are compns. and methods which relate to MHC Class II mol. presentation of antigenic epitopes which, under normal circumstances, would not be presented in association with MHC Class II mols. The invention relates to presentation in cells which normally express MHC Class II mols., as well as cells which can be induced to express MHC Class II mols. Adenoviral vectors are also constructed containing the transcription factor CIITA and/or interferon- $\gamma$  cDNAs for tumor protection by MHC Class II+/Ii-. By suppressing the expression of the Ii protein, this vast repertoire of peptides which have been transported into the endoplasmic reticulum to MHC Class I and subsequent presentation to CD8+ T lymphocytes, can bind to MHC Class II mols. for subsequent presentation to, and activation of, CD4+ T immunoregulatory cells. Embodiments relating to RNA interference of Ii are specifically disclosed. Sequences of Ii-specific siRNAs are presented.

L19 ANSWER 2 OF 13 CA COPYRIGHT 2006 ACS on STN

AN 142:183225 CA

TI RNA interference-mediated inhibition of gene expression using chemically modified short interfering nucleic acids

IN McSwiggen, James; Chowrira, Bharat; Beigelman, Leonid; Macejak, Dennis; Zinnen, Shawn; Pavco, Pamela; Haeberli, Peter; Morissey, David; Fosnaugh, Kathy; Jamison, Sharon; Usman, Nassim; Thompson, James; Vargeese, Chandra; Wang, Weimen; Chen, Tonqian; Vaish, Narendra

PA Sirna Therapeutics, Inc., USA

SO U.S. Pat. Appl. Publ., 204 pp., Cont.-in-part of U.S. Ser. No. 720,448. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 235

```
PATENT NO.
                          KIND
                                 DATE
                                             APPLICATION NO.
                                                                     DATE
ΡI
     US 2005020525
                                 20050127
                                                                     20040114
                           A1
                                             US 2004-757803
     AU 9851819
                          A1
                                 19980611
                                             AU 1998-51819
                                                                     19980112 <--
     AU 729657
                           B2
                                 20010208
     AU 9939188
                           A1
                                 19990916
                                             AU 1999-39188
                                                                     19990713 <--
     AU 769175
                           B2
                                 20040115
                                             AU 2000-56616
                                                                     20000911
     US 2005096284
                          A1
                                 20050505
                                             US 2004-783128
                                                                     20040220
     US 2005014172
                          A1
                                 20050120
                                             US 2004-798090
                                                                     20040311
     US 2005048529
                          A1
                                 20050303
                                             US 2004-800487
                                                                     20040315
     WO 2004092383
                          A2
                                 20041028
                                             WO 2004-US11320
                                                                     20040413
     WO 2004092383
                          A3
                                 20050210
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
     US 2005191638
                                             US 2004-824036
                          A1
                                 20050901
                                                                     20040414
     WO 2004111237
                                             WO 2004-US11848
                          A1
                                 20041223
                                                                     20040416
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
    US 2005032733
                                 20050210
                          Al
                                             US 2004-826966
                                                                     20040416
    WO 2004097020
                          A2
                                 20041111
                                             WO 2004-US12517
                                                                     20040423
    WO 2004097020
                          A3
                                 20060105
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
        RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
             BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
             ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
             SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
             TD, TG
    US 2005054598
                                 20050310
                          A1
                                             US 2004-830569
                                                                     20040423
    US 2005148530
                          A1
                                 20050707
                                             US 2004-831620
                                                                     20040423
    US 2005233996
                          A1
                                 20051020
                                             US 2004-832522
                                                                     20040426
    US 2005137153
                          A1
                                 20050623
                                             US 2004-840731
                                                                     20040506
    US 2005171039
                          A1
                                 20050804
                                             US 2004-844076
                                                                     20040511
    US 2005159376
                          A1
                                20050721
                                             US 2004-844072
                                                                     20040512
    AU 2004266311
                          A1
                                20050303
                                             AU 2004-266311
                                                                     20040524
    CA 2526831
                          AA
                                20050303
                                             CA 2004-2526831
                                                                     20040524
    EP 1627061
                          A2
                                 20060222
                                             EP 2004-776102
                                                                     20040524
        R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
    WO 2005045034
                          A2
                                20050519
                                             WO 2004-US17630
                                                                     20040603
    WO 2005045034
                          A3
                                20050811
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
```

```
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005137155
                            20050623
                      A1
                                        US 2004-861060
                                                                20040603
                      A2
EP 1675948
                            20060705
                                        EP 2004-754277
                                                                20040603
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 2005143333
                     A1
                            20050630
                                        US 2004-863973
                                                                20040609
US 2005171040
                     A1
                            20050804
                                        US 2004-864044
                                                                20040609
US 2005119211
                     A1
                            20050602
                                        US 2004-869638
                                                                20040616
US 2005119212
                            20050602
                                        US 2004-871222
                     A1
                                                                20040618
CA 2528963
                     AΑ
                            20050113
                                        CA 2004-2528963
                                                                20040625
WO 2005003350
                     A2
                            20050113
                                        WO 2004-US20516
                                                                20040625
WO 2005003350
                      C1
                            20050519
WO 2005003350
                     A3
                            20050804
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005209179
                                        US 2004-877889
                     A1
                            20050922
                                                                20040625
EP 1644498
                     A2
                            20060412
                                        EP 2004-756160
                                                                20040625
    R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 2005124566
                     A1
                            20050609
                                        US 2004-879867
                                                                20040628
US 2005130181
                     A1
                            20050616
                                        US 2004-881118
                                                                20040630
US 2006142225
                     A1
                            20060629
                                        US 2004-881580
                                                                20040630
US 2005124567
                     A1
                            20050609
                                        US 2004-883218
                                                                20040701
WO 2005007854
                            20050127
                                        WO 2004-US21997
                     A2
                                                                20040709
WO 2005007854
                     A3
                            20050818
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005007859
                                        WO 2004-US22247
                     A2
                            20050127
                                                                20040709
WO 2005007859
                     A3
                            20051201
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
```

```
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005124568
                      Al
                            20050609
                                        US 2004-888226
                                                                 20040709
US 2005222064
                      A1
                            20051006
                                        US 2004-888269
                                                                 20040709
                      A2
EP 1644500
                            20060412
                                         EP 2004-777833
                                                                 20040709
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    R:
        IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
WO 2005007855
                      A2
                            20050127
                                        WO 2004-US22658
                                                                 20040714
WO 2005007855
                      A3
                            20050324
    W:
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005124569
                      A1
                            20050609
                                        US 2004-892922
                                                                20040716
US 2005164224
                      A1
                            20050728
                                        US 2004-893010
                                                                20040716
US 2005070497
                      A1
                            20050331
                                        US 2004-894475
                                                                20040719
US 2005176663
                      A1
                            20050811
                                        US 2004-897902
                                                                20040723
                            20050908
US 2005196765
                      A1
                                        US 2004-898660
                                                                20040723
US 2005277608
                      A1
                            20051215
                                        US 2004-898311
                                                                20040723
US 2005182006
                      A1
                                        US 2004-903128
                            20050818
                                                                20040730
WO 2005014811
                      A2
                            20050217
                                        WO 2004-US25589
                                                                20040806
WO 2005014811
                      A3
                            20051222
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD,
                TG
US 2005159378
                                        US 2004-915896
                            20050721
                      A1
                                                                20040811
US 2005159379
                            20050721
                      A1
                                        US 2004-916030
                                                                20040811
US 2005158735
                      A1
                            20050721
                                        US 2004-916095
                                                                20040811
US 2005153914
                      A1
                            20050714
                                        US 2004-918969
                                                                20040816
US 2005164966
                      A1
                            20050728
                                        US 2004-918896
                                                                20040816
US 2005203040
                     A1
                            20050915
                                        US 2004-918987
                                                                20040816
US 2005176664
                     A1
                                        US 2004-919866
                            20050811
                                                                20040817
US 2005176665
                     A1
                            20050811
                                        US 2004-919964
                                                                20040817
US 2005233997
                     A1
                            20051020
                                        US 2004-919584
                                                                20040817
AU 2004288143
                     A1
                            20050519
                                        AU 2004-288143
                                                                20040818
CA 2541643
                     AA
                            20050519
                                        CA 2004-2541643
                                                                20040818
WO 2005045036
                     A2
                            20050519
                                        WO 2004-US27042
                                                                20040818
WO 2005045036
                     A3
                            20060302
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
```

```
SN, TD, TG
EP 1675950
                      A2
                            20060705
                                        EP 2004-781674
                                                                20040818
      AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
WO 2005045032
                                        WO 2004-US26941
                     A2
                            20050519
                                                                20040819
WO 2005045032
                      A3
                            20060302
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005045041
                     A2
                            20050519
                                        WO 2004-US27404
                                                                20040819
WO 2005045041
                     A3
                            20050818
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005136436
                            20050623
                     A1
                                        US 2004-923640
                                                                20040819
US 2005153915
                     A1
                            20050714
                                        US 2004-922544
                                                                20040819
US 2005159380
                     A1
                            20050721
                                        US 2004-922626
                                                                20040819
US 2005159382
                     Α1
                            20050721
                                        US 2004-923580
                                                                20040819
US 2005164967
                     A1
                            20050728
                                        US 2004-922034
                                                                20040819
US 2006142226
                     A1
                            20060629
                                        US 2004-921554
                                                                20040819
EP 1675951
                     A2
                            20060705
                                        EP 2004-781983
                                                                20040819
       AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 2005079610
                     A1
                            20050414
                                        US 2004-923115
                                                                20040820
                     A2
WO 2005035759
                            20050421
                                        WO 2004-US27294
                                                                20040820
WO 2005035759
                            20060202
                     C1
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005040379
                                        WO 2004-US27333
                     A2
                            20050506
                                                                20040820
WO 2005040379
                     A3
                            20060302
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
```

```
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
CA 2542527
                            20050519
                      AA
                                        CA 2004-2542527
                                                                20040820
CA 2542835
                      AA
                            20050519
                                        CA 2004-2542835
                                                                20040820
WO 2005045035
                      A2
                            20050519
                                        WO 2004-US26930
                                                                20040820
WO 2005045035
                      A3
                            20051208
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005045037
                      A2
                            20050519
                                        WO 2004-US27169
                                                                20040820
WO 2005045037
                      A3
                            20051103
WO 2005045037
                     B1
                            20051229
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
    W:
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005045038
                     A2
                            20050519
                                        WO 2004-US27231
                                                                20040820
WO 2005045038
                     Cl
                            20050714
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
                                       WO 2004-US27366
WO 2005045039
                     A2
                            20050519
                                                                20040820
WO 2005045039
                     C2
                            20050721
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
WO 2005045040
                     A2
                           20050519
                                       WO 2004-US27367
                                                               20040820
WO 2005045040
                     A3
                           20060223
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
       GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
       LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
       NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
```

```
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
         AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
         EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
         SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
         SN, TD, TG
WO 2005044981
                      A2
                            20050519
                                         WO 2004-US27403
                                                                 20040820
WO 2005044981
                      A3
                            20050922
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
         SN, TD, TG
US 2005153916
                      A1
                            20050714
                                         US 2004-923330
                                                                 20040820
US 2005159381
                            20050721
                    . A1
                                         US 2004-923522
                                                                 20040820
US 2005164968
                      A1
                            20050728
                                        US 2004-923329
                                                                 20040820
US 2005170371
                      A1
                            20050804
                                        US 2004-922340
                                                                 20040820
US 2005176666
                      A1
                            20050811
                                        US 2004-923182
                                                                 20040820
US 2005176024
                     .A1
                            20050811
                                        US 2004-923354
                                                                 20040820
US 2005176025
                      A1
                            20050811
                                         US 2004-923516
                                                                 20040820
US 2005182007
                      A1
                            20050818
                                        US 2004-922675
                                                                 20040820
US 2005182008
                      A1
                                        US 2004-923142
                            20050818
                                                                 20040820
US 2005182009
                      A1
                            20050818
                                        US 2004-923201
                                                                 20040820
US 2005187174
                      A1
                            20050825
                                        US 2004-923181
                                                                20040820
US 2005191618
                      A1
                            20050901
                                        US 2004-923473
                                                                20040820
US 2005196767
                      A1
                            20050908
                                        US 2004-923380
                                                                 20040820
US 2005227935
                            20051013
                      A1
                                        US 2004-923470
                                                                20040820
US 2005227936
                      A1
                            20051013
                                        US 2004-923475
                                                                20040820
US 2005233344
                            20051020
                      A1
                                        US 2004-923270
                                                                20040820
US 2005239731
                      A1
                            20051027
                                        US 2004-923379
                                                                20040820
US 2005256068
                      A1
                            20051117
                                        US 2004-923451
                                                                20040820
US 2005267058
                      A1
                            20051201
                                        US 2004-922761
                                                                20040820
US 2005288242
                      A1
                            20051229
                                        US 2004-923476
                                                                20040820
EP 1675949
                      A2
                            20060705
                                        EP 2004-781588
                                                                20040820
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
EP 1675953
                            20060705 EP 2004-816819
                      A2
    R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
WO 2005028650
                      A2
                            20050331
                                        WO 2004-US31012
                                                                20040915
WO 2005028650
                     A3
                            20051229
       AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
US 2005209180
                     A1
                            20050922
                                        US 2004-942560
                                                                20040915
EP 1670915
                                        EP 2004-816223
                     A2
                            20060621
                                                                20040915
    R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
        IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR
AU 2004274951
                                        AU 2004-274951
                     A1
                            20050331
                                                                20040916
CA 2537085
                            20050331
                     AA
                                        CA 2004-2537085
                                                                20040916
```

```
WO 2005028649
                           A1
                                 20050331
                                              WO 2004-US30488
                                                                      20040916
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 2005233998
                           A1
                                 20051020
                                              US 2004-944611
                                                                      20040916
     EP 1664299
                           A1
                                 20060607
                                              EP 2004-784372
                                                                      20040916
            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
     US 2005222066
                           A1
                                 20051006
                                              US 2004-962898
                                                                      20041012
     US 2005261219
                           A1
                                 20051124
                                              US 2004-1347
                                                                      20041201
     US 2005196781
                           A1
                                 20050908
                                              US 2004-14373
                                                                      20041215
     US 2006019913
                           A1
                                 20060126
                                              US 2005-31668
                                                                      20050106
     US 2006025361
                           A1
                                 20060202
                                                                      20050114
                                              US 2005-35813
     US 2005287128
                           A1
                                 20051229
                                              US 2005-54047
                                                                      20050209
     US 2005260620
                                 20051124
                                              US 2005-58582
                           A1
                                                                      20050215
     US 2005277133
                           A1
                                 20051215
                                              US 2005-63415
                                                                      20050222
     US 2005282188
                           A1
                                 20051222
                                              US 2005-98303
                                                                      20050404
     US 2006019917
                           A1
                                 20060126
                                              US 2005-140328
                                                                      20050527
PRAI US 2003-720448
                           A2
                                 20031124
                           A3
     AU 1995-26422
                                 19950518
     US 1996-623891
                           A
                                 19960325
     AU 1996-76662
                           A3
                                 19961025
     US 2000-181797P
                           P
                                 20000211
     US 2001-780533
                           B2
                                 20010209
                           A2
     WO 2001-US4273
                                 20010209
     US 2001-827395
                           B2
                                 20010405
                                 20010518
                           P
     US 2001-292217P
     US 2001-294140P
                           P
                                 20010529
                           P
     US 2001-296249P
                                 20010606
     US 2001-306883P
                           P
                                 20010720
     US 2001-916466
                           B1
                                 20010725
     US 2001-311865P
                           P
                                 20010813
     US 2001-930423
                                 20010815
     US 2001-318471P
                           P
                                 20010910
    US 2001-334461P
                           P
                                 20011130
     US 2002-358580P
                           P
                                 20020220
                           P
     US 2002-362016P
                                 20020306
     US 2002-363124P
                           ₽
                                 20020311
     WO 2002-US9187
                           A2
                                 20020326
                           A2
     WO 2002-US10512
                                 20020403
    US 2002-374722P
                           P
                                 20020422
    US 2002-151116
                           A2
                                 20020517
    WO 2002-US15876
                           A2
                                 20020520
                           A2
     US 2002-157580
                                 20020529
    WO 2002-US16840
                           A2
                                 20020529
     WO 2002-US17674
                           A2
                                 20020529
                           A2
     US 2002-163552
                                 20020606
     US 2002-386782P
                           P
                                 20020606
    US 2002-393796P
                           P
                                 20020703
     US 2002-393924P
                           P
                                 20020703
     US 2002-396600P
                           P
                                 20020717
     US 2002-396905P
                           P
                                 20020718
                           A2
     US 2002-201394
                                 20020722
     US 2002-398036P
                           P
                                 20020723
    US 2002-205309
                           A2
                                 20020725
    US 2002-206705
                           A2
                                 20020726
```

US 2002-399348P	P	20020729		
US 2002-401093P	P	20020805		
US 2002-401104P	P	20020805		
US 2002-401104P	P	20020805		
		<del>-</del>		
US 2002-225023	A2	20020821		
US 2002-406784P	P	20020829		
US 2002-408378P	P	20020905		
US 2002-409293P	. <b>P</b>	20020909		
US 2002-409493P	P	20020909		
US 2002-238700	A2	20020910		•
US 2002-409785P	P	20020911		
US 2002-411275P	P	20020917		
			•	
US 2002-411707P	P	20020918		
US 2002-251117	A2	20020919		
US 2002-412304P	P	20020920		
US 2002-413714P	P	20020926		
US 2002-418655P	P	20021015		
US 2002-277494	B2	20021021		
US 2002-287949	A2	20021104		
US 2002-425559P	P	20021104		
US 2002-427467P	P	20021119		
US 2002-306747	A2	20021127		
US 2002-429359P	P	20021128		
US 2002-431105P	P	20021205		
US 2003-439922P	P	20030114		
US 2003-440129P	P	20030115		
WO 2003-US2510	A2	20030128		
WO 2003-US3473	A2	20030205		
WO 2003-US3662				
	A2	20030206		
WO 2003-US4034	A2	20030211		
WO 2003-US4088	A2	20030211		
WO 2003-US4123	A2	20030211		
WO 2003-US4347	A2	20030211		
WO 2003-US4566	A2	20030211		
WO 2003-US7273	A2	20030211		
WO 2003-US4250	A2	20030213		
WO 2003-US4317	A2	20030213		
WO 2003-US4397	A2	20030213		
		_		
WO 2003-US4402	A2	20030213		
WO 2003-US4448	A2	20030213		
WO 2003-US4710	<b>A2</b>	20030218	•	
WO 2003-US4738	A2	20030218		
WO 2003-US4907	<b>A2</b>	20030218		
WO 2003-US4908	A2	20030218		
WO 2003-US4909	A2	20030218		
WO 2003-US4741	A2	20030220		
WO 2003-US4951	A2	20030220		
WO 2003-US5022				
	A2	20030220		
WO 2003-US5028	A2	20030220		
WO 2003-US5043	A2	20030220		
WO 2003-US5044	A2	20030220		
WO 2003-US5045	<b>A2</b>	20030220		
WO 2003-US5162	A2	20030220		
WO 2003-US5190	Α	20030220		
WO 2003-US5234	A2	20030220		
WO 2003-US5326	A2	20030220		
WO 2003-US5346	A2	20030220		•
US 2003-053346 US 2003-462874P				
	P	20030415		
US 2003-417012	B2	20030416		
US 2003-420194	A2	20030422		
WO 2003-US12626	A2	20030422		
US 2003-422704	B2	20030424		
US 2003-424339	Α	20030425		
US 2003-427160	A2	20030430		

US 2003-430882	A2	20030506
US 2003-444853	A2	20030523
US 2003-607933	Α	20030627
US 2003-485667P	P	20030709
US 2003-486729P	P	20030711
	_	
US 2003-487214P	P	20030714
US 2003-493561P	P	20030808
US 2003-496655P	P	20030820
US 2003-652791	A2	20030829
US 2003-664767	Α	20030916
US 2003-665255	A2	20030916
US 2003-667271	A	20030916
US 2003-664668	A2	20030918
US 2003-665951	A2	20030918
US 2003-670011	A2	20030923
US 2003-683990		
	A2	20031010
US 2003-512701P	P	20031020
US 2003-693059	A2	20031023
US 2003-698311	Α	20031031
US 2003-712633	A2	20031113
US 2003-724270	A2	20031126
US 2003-726236	A2	20031202
US 2003-727780	A2	
		20031203
US 2003-738128	A2	20031218
US 2004-758155	A2	20040112
US 2004-757803	A2	20040114
US 2004-764957	A2	20040126
US 2004-543480P	P	20040210
US 2004-780447	Α	20040213
US 2004-783128	A2	20040220
US 2004-798090	A2	20040311
US 2004-800487	A2	20040315
US 2004-824036	A2	20040414
US 2004-825485	A2	20040415
		_
US 2004-826966	A2	20040416
WO 2004-US11848	<b>A2</b>	20040416
US 2004-830569	A2	20040423
US 2004-831620	A2	20040423
WO 2004-US12517	A2	20040423
US 2004-832522	A2	20040426
WO 2004-US13456	A	20040430
US 2004-570086P	P	20040511
US 2004-844076	A	20040511
US 2004-844072	Α	20040512
US 2004-16390	Α	20040524
WO 2004-US16390	W	20040524
WO 2004-US17630	W	20040603
US 2004-863973	A2	20040609
US 2004-864044	Α	20040609
WO 2004-US20516	W	
		20040625
WO 2004-US21997	W	20040709
US 2004-894475	A2	20040719
US 2004-919866	Α	20040817
WO 2004-US27042	W	20040818
		_
WO 2004-US27404	W	20040819
US 2004-922675	A2	20040820
US 2004-923475	A2	20040820
US 2004-923536	A2	20040820
WO 2004-US26930	W	20040820
WO 2004-US27333	W	20040820
WO 2004-US27367	W	20040820
WO 2004-US27403	W	20040820
WO 2004-US31012	W	20040915
US 2004-944611	<b>A2</b>	20040916

WO	2004-US30488	W	20040916
US	2005-31668	A1	20050106
US	2005-39680	A2	20050118
WO	2005-US4270	A2	20050209
US	2005-98303	A2	20050404

AB The present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to synthetic chemical modified small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid sequences. Introduction of chemical modified nucleotides into nucleic acid mols. provides a powerful tool in overcoming potential limitations of in vivo stability and bioavailability inherent to native RNA mols. Unlike native unmodified siRNA, chemical modified siNA can also minimize the possibility of activating interferon activity in humans. Modifications are described including pyrimidine or purine nucleotides with 2'-deoxy-2'-fluoro or 2'-O-Me groups, phosphorothioate backbone modification, terminal residues comprising inverted deoxy thymidine or inverted deoxy abasic moieties, linking the sense and antisense strands with glyceryl succinate or dodecanoic acid or other linkers, and conjugation of targeting ligands (N-acetylgalactosamine, pteroic acid, peptides, or phospholipids) to the oligonucleotide termini. Thus, the serum stability of siNA constructs consisting of all RNA nucleotides containing two thymidine nucleotide overhangs have a half-life in human serum of 15 s, whereas chemical modified siNA constructs remained stable in serum for 1 to 3 days depending on the extent of modification. The small nucleic acid mols. are useful in the treatment of any disease or condition that responds to modulation of gene expression or activity in a cell, tissue, or organism. Three nuclease-resistant siNA mols. targeting site 1580 of hepatitis B virus RNA are designed using Stab 7/8 chemical and a 5'-terminal conjugate moiety (a branched cholesterol conjugate, a branched phospholipid conjugate, and a polyethylene glycol conjugate) showed significant stability in human and mouse serum (t1/2 = 10-408 h) and human liver extract (t1/2 = 28-43 h); the most stable siNA with all purine positions in the antisense strand with 2'-O-Me nucleotides had a half-life of 816 h in human liver extract

L19 ANSWER 3 OF 13 CA COPYRIGHT 2006 ACS on STN

AN 141:319980 CA

TI RNA interference-mediated inhibition of gene expression using chemically modified short interfering nucleic acids

IN Mcswiggen, James; Chowrira, Bharat; Beigelman, Leonid; Macejak, Dennis; Zinnen, Shawn; Pavco, Pamela; Haeberli, Peter; Morrissey, David; Fosnaugh, Kathy; Jamison, Sharon; Usman, Nassim; Thompson, James; Vargeese, Chandra; Wang, Weimin; Chen, Tongqian; Vaish, Narendra

PA USA

SO U.S. Pat. Appl. Publ., 407 pp., Cont.-in-part of U.S. Ser. No. 427,160. CODEN: USXXCO

DT Patent

LA English

FAN.CNT 235

	PATENT NO.	KIND DATE	APPLICATION NO.	DATE
PI	US 2004192626	A1 20040930	US 2003-444853	20030523
	AU 9851819	A1 19980611	AU 1998-51819	19980112 <
	AU 729657	B2 20010208		
	AU 9939188	A1 19990916	AU 1999-39188	19990713 <
	AU 769175	B2 20040115	AU 2000-56616	20000911
	WO 2002094185	A2 20021128	WO 2002-US15876	20020520 <
	W: AE, AG, A	L, AM, AT, AU, AZ,	BA, BB, BG, BR, BY, BZ,	CA, CH, CN,
	CO, CR, C	U. CZ. DE. DK. DM.	DZ. EC. EE. ES. FT. GB.	•

```
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
        PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
        UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
        CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
        BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2003070918
                                        WO 2003-US5346
                      A2
                            20030828
                                                                20030220 <--
WO 2003070918
                      A3
                            20040708
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
    W:
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
        PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
        UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
        KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
        FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
        BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
WO 2003074654
                      A2
                                        WO 2003-US5028
                            20030912
                                                                20030220 <--
WO 2003074654
                     A3
                            20040205
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
        PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
        UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
        KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
        FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
        BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004110296
                     A1
                            20040610
                                        US 2003-427160
                                                                20030430
WO 2003106476
                                        WO 2003-US18911
                     A1
                            20031224
                                                                20030616 <--
WO 2003106476
                     C1
                            20040610
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
        CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
        GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
        LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
        PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR,
        TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG,
                                                         ZW, AM, AZ, BY,
        KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
        FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
        BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
AU 2003245512
                           20031231
                     Al
                                        AU 2003-245512
                                                               20030616 <--
US 2005106726
                     Al
                           20050519
                                        US 2003-652791
                                                               20030829
US 2004209831
                           20041021
                     A1
                                        US 2003-667271
                                                               20030916
US 2005080031
                     A1
                           20050414
                                        US 2003-724270
                                                               20031126
US 2005233329
                     A1
                           20051020
                                        US 2003-727780
                                                               20031203
US 2005096284
                     A1
                           20050505
                                       US 2004-783128
                                                               20040220
US 2005014172
                     A1
                           20050120
                                        US 2004-798090
                                                               20040311
US 2005048529
                     A1
                           20050303
                                       US 2004-800487
                                                               20040315
WO 2004092383
                     A2
                           20041028
                                       WO 2004-US11320
                                                               20040413
WO 2004092383
                     A3
                           20050210
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
   RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
        BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
        ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
        SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
```

```
TD, TG
US 2005191638
                      A1
                             20050901
                                         US 2004-824036
                                                                 20040414
WO 2004111237
                                         WO 2004-US11848
                      A1
                             20041223
                                                                 20040416
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
         CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
         GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
         TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
         BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
         ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
         SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
         TD, TG
US 2005032733
                      A1
                            20050210
                                         US 2004-826966
                                                                 20040416
WO 2004097020
                      A2
                            20041111
                                         WO 2004-US12517
                                                                 20040423
WO 2004097020
                      A3
                            20060105
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
        BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
        ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
        SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
        TD, TG
US 2005054598
                      A1
                            20050310
                                         US 2004-830569
                                                                 20040423
US 2005148530
                      A1
                            20050707
                                         US 2004-831620
                                                                 20040423
US 2005233996
                            20051020
                                         US 2004-832522
                      A1
                                                                 20040426
US 2005137153
                            20050623
                      A1
                                         US 2004-840731
                                                                 20040506
US 2005171039
                      A1
                            20050804
                                         US 2004-844076
                                                                 20040511
                            20050721
US 2005159376
                      A1
                                         US 2004-844072
                                                                 20040512
AU 2004266311
                      A1
                            20050303
                                         AU 2004-266311
                                                                 20040524
CA 2526831
                      AA
                            20050303
                                         CA 2004-2526831
                                                                 20040524
WO 2005019453
                                        WO 2004-US16390
                      A2
                            20050303
                                                                20040524
WO 2005019453
                            20050623
                      A3
        AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
        CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
        GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
        LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
        NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
        TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
    RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
        AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
        EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
        SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
        SN, TD, TG
EP 1627061
                      A2
                            20060222
                                        EP 2004-776102
                                                                20040524
        AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
    R:
        IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
US 2005137155
                     Al
                            20050623
                                        US 2004-861060
                                                                20040603
US 2005143333
                            20050630
                     A1
                                        US 2004-863973
                                                                20040609
US 2005171040
                     A1
                            20050804
                                        US 2004-864044
                                                                20040609
US 2005119211
                                        US 2004-869638
                     Al
                            20050602
                                                                20040616
US 2005119212
                     A1
                            20050602
                                        US 2004-871222
                                                                20040618
US 2005209179
                     A1
                            20050922
                                        US 2004-877889
                                                                20040625
US 2005124566
                     A1
                                        US 2004-879867
                            20050609
                                                                20040628
                            20050616
US 2005130181
                     A1
                                        US 2004-881118
                                                                20040630
US 2006142225
                     A1
                            20060629
                                        US 2004-881580
                                                                20040630
US 2005124567
                     A1
                                        US 2004-883218
                            20050609
                                                                20040701
US 2005124568
                                        US 2004-888226
                            20050609
                     A1
                                                                20040709
US 2005222064
                            20051006
                                        US 2004-888269
                     A1
                                                                20040709
```

	US	2005124569	A1	20050609	US	2004-892922	20040716
	US	2005164224	A1	20050728	US	2004-893010	20040716
	US	2005070497	A1	20050331	US	2004-894475	20040719
	US	2005176663	A1	20050811	US	2004-897902	20040723
	US	2005196765	A1	20050908	US	2004-898660	20040723
	US	2005277608	A1	20051215	US	2004-898311	20040723
	US	2005182006	A1	20050818	US	2004-903128	20040730
	US	2005159378	A1	20050721	US	2004-915896	20040811
	US	2005159379	A1	20050721	US		20040811
	US		A1	20050721	US	2004-916095	20040811
	US	2005153914	A1	20050714	US	<del>-</del>	20040816
	US		A1	20050728	US		20040816
	US		A1	20050915	US		20040816
	US	2005176664	A1	20050811	US		20040817
	US	2005176665	A1	20050811	US		20040817
	US	2005233997 2005136436	A1	20051020	US		20040817
	US	2005153915	A1 A1	20050623	US		20040819
	US	2005153315	A1	20050714 20050721	US US		20040819 20040819
	US	2005159382	A1	20050721	US		20040819
	US	2005164967	A1	20050721	US	2004-923380	20040819
	US	2005104307	A1	20050728	US	2004-921554	20040819
		2005079610	A1	20050414		2004-921334	20040819
	US	2005173016	A1	20050414	US		20040820
	US	2005159381	A1	20050714	US	2004-923530	20040820
		2005164968	A1	20050721		2004 923322	20040820
	US		A1	20050804		2004-922340	20040820
		2005176666	A1	20050811		2004-923182	20040820
	US	2005176024	A1	20050811		2004-923354	20040820
	US	2005176025	A1	20050811	US		20040820
	US	2005182007	A1	20050818	US	2004-922675	20040820
	US	2005182008	A1	20050818	US	2004-923142	20040820
	US	2005182009	A1	20050818	US	2004-923201	20040820
	US	2005187174	A1	20050825	US	2004-923181	20040820 1
	US	2005191618	A1	20050901	US	2004-923473	20040820
	US	2005196767	A1	20050908	US	2004-923380	20040820
	US	2005227935	A1	20051013	US	2004-923470	20040820
	US	2005227936	A1	20051013	US	2004-923475	20040820
	US	2005233344	A1	20051020		2004-923270	20040820
	US	2005239731	A1	20051027		2004-923379	20040820
	US	2005256068	A1	20051117	US		20040820
		2005267058	A1	20051201	US	2004-922761	20040820
	US US	2005288242 2005209180	A1	20051229		2004-923476	20040820
		2005233998	A1 A1	20050922 20051020	US	2004 - 942560	20040915
		2005233336	A1	20051020		2004-944611 2004-962898	20040916
		2005261219	A1	20051008		2004-362838	20041012 20041201
		2005209182	A1	20051124		2004-1347	20041201
		2005196781	Al	20050922		2004-11913	20041214
		2006019913	A1	20060126		2005-31668	200511213
		2006025361	A1	20060202		2005-35813	20050100
		2005287128	A1	20051229		2005-54047	20050219
	US	2005260620	A1	20051124		2005-58582	20050215
	US	2005277133	A1	20051215		2005-63415	20050222
	US	2005282188	A1	20051222		2005-98303	20050404
	US	2006019917	A1	20060126		2005-140328	20050527
PRAI	WO	2002-US15876	A2	20020520			
		2003-US5028	A2	20030220			
		2003-US5346	A2	20030220	•		
		2003-417012	A1	20030416			
		2003-422704	A2	20030424			
		2003-427160	A2	20030430			
		1995-26422	A3	19950518			
	US	1996-623891	A	19960325			

ΑU	1996-76662	A3	19961025
US	2000-181797P	P	20000211
US	2001-780533	B2	20010209
WO		A2	20010209
US		B2	20010405
	2001-292217P	P	20010518
US		P	20010510
	2001-2941401 2001-296249P	P	20010606
	2001-290249P 2001-306883P	P	20010303
	2001-3068632	B1	20010725
	2001-311865P	P	20010723
	2001-3118652		
		B2	20010815
US		P	20010910
	2001-334461P	P	20011130
	2002-358580P	P	20020220
US		P	20020306
US		P	20020311
WO	<del>-</del> -	A2	20020326
WO		A2	20020403
US		P	20020422
US	· · · · ·	A2	20020517
US		A2	20020529
WO	2002-US16840	A2	20020529
WO	2002-US17674	A2	20020529
US	2002-163552	A2	20020606
US	2002-386782P	P	20020606
US	2002-389198P	P	20020617
US	2002-393796P	P	20020703
US	2002-393924P	P	20020703
US	2002-396600P	P	20020717
US	2002-396905P	P	20020718
US	2002-201394	A2	20020722
US	2002-398036P	P	20020723
US	2002-205309	A2	20020725
US	2002-206705	A2	20020726
US	2002-399348P	P	20020729
US	2002-401093P	P	20020805
	2002-401104P	P	20020805
	2002-404039P	P	20020815
	2002-225023	A2	20020821
	2002-406784P	P	20020829
	2002-408378P	P	20020905
	2002-409293P	P	20020909
	2002-409493P	P	20020909
	2002-238700	A2	20020910
	2002-409785P	P	20020910
	2002-411275P	P	20020917
	2002-411707P	P	20020917
	2002-251117	A2	20020919
US		P	20020920
	2002 4123041 2002-413714P	P	20020926
	2002-418/14P	P	20021015
	2002-410055F	B2	20021015
	2002-277494	A2	20021021
	2002-287949 2002-425559P		
	2002-425559P 2002-427467P	P	20021112
	2002-4274672	P	20021119
		A2	20021127
		P	20021128
	2002-431105P	P	20021205
	2003-439922P	P	20030114
	2003-440129P	P	20030115
	2003-US2510	A2	20030128
MO	2003-US3473	A2	20030205
WO	2003-US3662	A2	20030206

WO	2003-US4034	A2	20030211
WO		A2	20030211
WO		A2	20030211
WO		A2	20030211
WO		A2	20030211
WO	2003-US7273	<b>A2</b>	20030211
WO	2003-US4250	A2	20030213
WO	2003-US4317	A2	20030213
WO	2003-US4397	A2	20030213
WO		A2	20030213
WO		A2	20030213
WO		A2	20030213
WO		A2	. 20030218
WO		A2	20030218
WO	2003-US4908	A2	20030218
WO	2003-US4909	<b>A2</b>	20030218
WO	2003-US4741	<b>A2</b>	20030220
WO	2003-US4951	A2	20030220
WO	2003-US5022	A2	20030220
WO		A2	20030220
WO		A2	20030220
WO		A2	20030220
		A2	20030220
WO	2003-US5190	Α	20030220
WO	2003-US5234	A2	20030220
WO	2003-US5326	A2	20030220
US	2003-462874P	P	20030415
US	2003-420194	A2	20030422
	2003-US12626	A2	20030422
	2003-424339		
		A	20030425
	2003-430882	A2	20030506
	2003-444853	A	20030523
	2003-US18911	W	20030616
US	2003-607933	A2	20030627
US	2003-485667P	P	20030709
US	2003-486729P	P	20030711
US	2003-652791	A2	20030829
	2003-664767	B2	20030916
	2003-665255	A2	
	2003-667271		20030916
		A2	20030916
	2003-664668	A2	20030918
	2003-665951	<b>A2</b>	20030918
US	2003-670011	A2	20030923
US	2003-683990	<b>A2</b>	20031010
US	2003-512701P	P	20031020
US	2003-693059	A2	20031023
	2003-698311	A2	20031031
	2003-712633	A2	20031031
	2003 - 720448		
		A2	20031124
	2003-724270	A2	20031126
	2003-726236	A2	20031202
US	2003-727780	A2	20031203
US	2003-738128	A2	20031218
US	2004 - 758155	A2	20040112
US	2004-757803	<b>A2</b>	20040114
	2004-764957	A2	20040126
	2004 704337 2004 - 543480P	P P	
			20040210
	2004 - 780447	A	20040213
	2004-783128	A2	20040220
	2004-798090	A2	20040311
US	2004-800487	A2	20040315
US	2004-824036	<b>A2</b>	20040414
·US	2004-825485	<b>A2</b>	20040415
	2004-826966	A2	20040416
-			<del></del>

•

.

WO	2004-US11848	A2	20040416
US	2004-830569	A2	20040423
US	2004-831620	A2	20040423
WO	2004-US12517	A2	20040423
US	2004-832522	A2	20040426
WO	2004-US13456	A2	20040430
US	2004-570086P	P	20040511
US	2004-844076	A2	20040511
US	2004-844072	A2	20040512
WO	2004-US16390	W	20040524
US	2004-863973	A2	20040609
US	2004-864044	A2	20040609
US	2004-894475	A2	20040719
US	2004-922675	A2	20040820
US	2004-923475	A2	20040820
US	2004-923536	A2	20040820
US	2004-944611	A2	20040916
US	2005-31668	A1	20050106
US	2005-39680	· A2	20050118
WO	2005-US4270	A2	20050209
US	2005-98303	A2	20050404

ABThe present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to synthetic chemical modified small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid Introduction of chemical modified nucleotides into nucleic acid mols. provides a powerful tool in overcoming potential limitations of in vivo stability and bioavailability inherent to native RNA mols. Unlike native unmodified siRNA, chemical modified siNA can also minimize the possibility of activating interferon activity in humans. Modifications are described including pyrimidine or purine nucleotides with 2'-deoxy-2'-fluoro or 2'-O-Me groups, phosphorothioate backbone modification, terminal residues comprising inverted deoxy thymidine or inverted deoxy abasic moieties, linking the sense and antisense strands with glyceryl succinate or dodecanoic acid or other linkers, and conjugation of targeting ligands (N-acetylgalactosamine, pteroic acid, peptides, or phospholipids) to the oligonucleotide termini. Thus, the serum stability of siNA constructs consisting of all RNA nucleotides containing two thymidine nucleotide overhangs have a half-life in human serum of 15 s, whereas chemical modified siNA constructs remained stable in serum for 1 to 3 days depending on the extent of modification. The small nucleic acid mols. are useful in the treatment of any disease or condition that responds to modulation of gene expression or activity in a cell, tissue, or organism. Three nuclease-resistant siNA mols. targeting site 1580 of hepatitis B virus RNA are designed using Stab 7/8 chemical and a 5'-terminal conjugate moiety (a branched cholesterol conjugate, a branched phospholipid conjugate, and a polyethylene glycol conjugate) showed significant stability in human and mouse serum (t1/2 = 10-408 h) and human liver extract (t1/2 = 28-43 h); the most stable siNA with all purine positions in the antisense strand with 2'-O-Me nucleotides had a half-life of 816 h in human liver extract

L19 ANSWER 4 OF 13 CA COPYRIGHT 2006 ACS on STN

AN 139:207762 CA

TI RNA interference mediated inhibition of gene expression using chemically modified short interfering nucleic acid

IN McSwiggen, James; Beigelman, Leonid; Macejak, Dennis; Zinnen, Shawn;
Pavco, Pamela; Morrissey, David; Fosnaugh, Kathy; Mokler, Victor; Jamison,
Sharon

PA Ribozyme Pharmaceuticals, Incorporated, USA

SO PCT Int. Appl., 204 pp. CODEN: PIXXD2 DT Patent English LA FAN.CNT 235 APPLICATION NO. PATENT NO. KIND DATE DATE PIWO 2003070918 **A2** WO 2003-US5346 20030828 20030220 <--WO 2003070918 **A3** 20040708 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 9851819 A1 19980611 AU 1998-51819 19980112 <--AU 729657 **B**2 20010208 AU 9939188 A1 19990916 AU 1999-39188 19990713 <--**B2** AU 769175 20040115 AU 2000-56616 20000911 CA 2459532 ΑĄ 20030828 CA 2003-2459532 20030220 <--AU 2003221258 **A1** 20030909 AU 2003-221258 20030220 <--GB 2397818 A1 20040804 GB 2004-6022 20030220 GB 2397818 **B2** 20050309 20040922 EP 1458741 **A2** EP 2003-716126 20030220 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK 20050616 JP 2005517438 **T2** JP 2003-569811 20030220 US 2006127891 A1 20060615 20030425 US 2003-424339 'US 2004110296 **A1** US 2003-427160 20040610 20030430 US 2004192626 US 2003-444853 A1 20040930 20030523 WO 2003106476 A1 20031224 WO 2003-US18911 20030616 <--WO 2003106476 C1 20040610 AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, W: CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG AU 2003245512 20031231 **A1** AU 2003-245512 20030616 <--US 2005106726 20050519 **A1** US 2003-652791 20030829 20050414 US 2005080031 **A1** US 2003-724270 20031126 US 2005233329 20051020 **A1** US 2003-727780 20031203 US 2004249178 20041209 **A1** US 2004-780447 20040213 US 2005096284 **A**1 20050505 US 2004-783128 20040220 20050120 US 2005014172 **A1** US 2004-798090 20040311 US 2005048529 **A**1 20050303 US 2004-800487 20040315 US 2005191638 A1 20050901 US 2004-824036 20040414 US 2005032733 **A1** 20050210 US 2004-826966 20040416 US 2005054598 **A**1 20050310 US 2004-830569 20040423 US 2005148530 A1 US 2004-831620 20050707 20040423 US 2005233996 A1 20051020 US 2004-832522 20040426 US 2005137153 A1 20050623 US 2004-840731 20040506 US 2005171039 **A**1 20050804 US 2004-844076 20040511

US 2005159376

US 2005137155

US 2005143333

A1

**A**1

A1

20050721

20050623

20050630

US 2004-844072

US 2004-861060

US 2004-863973

20040512

20040603

20040609

US 2005171040	<b>A1</b>	20050804	US 2004-864044	20040609
US 2005119211	<b>A</b> 1	20050602	US 2004-869638	20040616
US 2005119212	<b>A</b> 1	20050602	US 2004-871222	20040618
US 2005209179	A1	20050922	US 2004-877889	20040625
US 2005124566	A1	20050609	US 2004-879867	20040628
US 2005130181	<b>A1</b>	20050616	US 2004-881118	20040630
US 2006142225	<b>A1</b>	20060629	US 2004-881580	20040630
US 2005124567	<b>A1</b>	20050609	US 2004-883218	20040701
US 2005124568	<b>A1</b>	20050609	US 2004-888226	20040709
US 2005222064	A1	20051006	US 2004-888269	20040709
US 2005124569	A1	20050609	US 2004-892922	20040716
US 2005164224	<b>A1</b>	20050728	US 2004-893010	20040716
US 2005070497	A1	20050331	US 2004-894475	20040719
US 2005176663	A1	20050811	US 2004-897902	20040723
US 2005196765	<b>A1</b>	20050908	US 2004-898660	20040723
US 2005277608	A1	20051215	US 2004-898311	20040723
US 2005182006	A1	20050818	US 2004-903128	20040730
US 2005159378	A1	20050721	US 2004-915896	20040811
US 2005159379	A1.	20050721	US 2004-916030	20040811
US 2005158735	A1	20050721	US 2004-916095	20040811
US 2005153914	A1	20050714	US 2004-918969	20040816
US 2005164966	A1	20050728	US 2004-918896	20040816
US 2005203040	A1	20050915	US 2004-918987	20040816
US 2005176664	A1	20050811	US 2004-919866	20040817
US 2005176665 US 2005233997	A1	20050811	US 2004-919964	20040817
US 2005233997 US 2005136436	A1 A1	20051020	US 2004-919584	20040817
US 2005153915	A1	20050623 20050714	US 2004-923640 US 2004-922544	20040819
US 2005159380	A1	20050714	US 2004-922626	20040819 20040819
US 2005159382	A1	20050721	US 2004-923580	20040819
US 2005164967	A1	20050721	US 2004-923330	20040819
US 2006142226	A1	20050720	US 2004-921554	20040819
US 2005079610	A1	20050414	US 2004-923115	20040820
US 2005153916	, A1	20050714	US 2004-923330	20040820
US 2005159381	A1	20050721	US 2004-923522	20040820
US 2005164968	A1	20050728	US 2004-923329	20040820
US 2005170371	<b>A1</b>	20050804	US 2004-922340	20040820
US 2005176666	A1	20050811	US 2004-923182	20040820
US 2005176024	A1	20050811	US 2004-923354	20040820
US 2005176025	A1	20050811	· US 2004-923516	20040820
US 2005182007	A1	20050818	US 2004-922675	20040820
US 2005182008	A1	20050818	US 2004-923142	20040820
US 2005182009	A1	20050818	US 2004-923201	20040820
US 2005187174	A1	20050825	US 2004-923181	20040820
US 2005191618	A1	20050901	US 2004-923473	20040820
US 2005196767	A1	20050908	US 2004-923380	20040820
US 2005227935	A1	20051013	US 2004-923470	20040820
US 2005227936	A1	20051013	US 2004-923475	20040820
US 2005233344	A1	20051020	US 2004-923270	20040820
US 2005239731	A1	20051027	US 2004-923379	20040820
US 2005256068	A1	20051117	US 2004-923451	20040820
US 2005267058	A1	20051201	US 2004-922761	20040820
US 2005288242	A1	20051229	US 2004-923476	20040820
US 2005209180	A1	20050922	US 2004-942560	20040915
US 2005233998 US 2005222066	A1	20051020	US 2004-944611	20040916
US 2005222066 US 2005266422	A1	20051006 20051201	US 2004-962898	20041012
US 2005266422 US 2005261219	A1 A1	20051201	US 2004-981966 US 2004-1347	20041105
US 2005201219 US 2005209182	A1	20051124	US 2004-1347 US 2004-11913	20041201 20041214
US 2005196781	A1	20050922	US 2004-11913 US 2004-14373	20041214
US 2005190701 US 2006019913	A1	20050908	US 2004-143/3	20041215
US 2006025361	A1	20060120	US 2005-35813	20050108
US 2005287128	A1	20051229	US 2005-54047	20050114
US 2005260620	A1	20051124	US 2005-58582	20050215
		<b></b>		

•

	US 2005277133	A1	20051215	US 2005-63415	20050222
	US 2005282188	A1	20051222	US 2005-98303	20050404
DD 3 T	US 2006019917	A1	20060126	US 2005-140328	20050527
PRAI		P	20020220		
	US 2002-363124P US 2002-386782P	P P	20020311 20020606		
	US 2002-386782P	p	20020808		
	US 2002-408378P	P	20020025		
	AU 1995-26422	A3	19950518		
	US 1996-623891	A	19960325		
	AU 1996-76662	<b>A3</b>	19961025		
	US 2000-181797P	P	20000211		
	US 2001-780533	B2	20010209		
	WO 2001-US4273	A2	20010209		
	US 2001-827395	B2	20010405		
	US 2001-292217P	P	20010518		
	US 2001-294140P US 2001-296249P	P P	20010529 20010606		
	US 2001-290249P	P	20010000		
	US 2001-916466	B1	20010725	•	
	US 2001-311865P	P	20010813		
	US 2001-930423	B2	20010815		
	US 2001-318471P	. P	20010910		
	US 2001-334461P	P	20011130		
	US 2002-362016P	P	20020306		
	WO 2002-US9187	A2	20020326		
	WO 2002-US10512	A2	20020403		
	US 2002-374722P US 2002-151116	P A2	20020422 20020517		
	WO 2002-US15876	A2	20020517		
	US 2002-157580	A2	20020520		•
	WO 2002-US16840	A2	20020529		
	WO 2002-US17674	A2	20020529		
	US 2002-163552	A2	20020606		
	US 2002-389198P	P	20020617		1
	US 2002-393796P	P	20020703		
	US 2002-393924P	P	20020703		
	US 2002-396600P US 2002-396905P	P P	20020717 20020718		
	US 2002-201394	A2	20020718		
	US 2002-398036P	P	20020722		
	US 2002-205309	A2	20020725		
	US 2002-206705	A2	20020726		
	US 2002-399348P	<b>P</b> .	20020729		
	US 2002-401093P	P	20020805		
	US 2002-401104P	P	20020805		
	US 2002-404039P	P	20020815		
	US 2002-225023 US 2002-409293P	A2	20020821		
	US 2002-409293P	P P	20020909 20020909		
	US 2002-238700	A2	20020909		
	US 2002-409785P	P	20020911		
	US 2002-411275P	P	20020917		
	US 2002-411707P	P	20020918		
	US 2002-251117	A2	20020919		
	US 2002-412304P	P	20020920		
	US 2002-413714P	P	20020926		
	US 2002-418655P	P	20021015		
	US 2002-277494 US 2002-287949	B2 A2	20021021		
	US 2002-425559P	AZ P	20021104 20021112		
	US 2002-427467P	P	20021112		
	US 2002-306747	A2	20021117		
	US 2002-429359P	P	20021128		

HC	2002-431105P	P	20021205
US	2003-439922P	P	20030114
US	2003-440129P	P	20030115
WO	2003-US2510	A2	20030128
WO	2003-US3473 .	<b>A2</b>	20030205
WO	2003-US3662	A2	20030206
WO	2003-US4034	A2	20030211
WO	2003-US4088	A2	20030211
WO	2003-US4123	A2	20030211
_			
WO		A2	20030211
WO	2003-US4566	A2	20030211
WO	2003-US7273	A2	20030211
	2003-US4250	A2	20030213
WO	2003-US4317	<b>A2</b>	20030213
WO	2003-US4397	A2	20030213
WO		A2	20030213
WO	2003-US4448	A2	20030213
WO	2003-US4710	A2	20030218
WO	2003-US4738	A2	20030218
WO	2003-US4907	A2	20030218
WO	2003-US4908	A2	20030218
WO	2003-US4909	A2	20030218
WO	2003-US4741	A2	20030220
WO	2003-US4951	A2	20030220
WO	2003-US5022	A2	20030220
WO	2003-US5028	A2	20030220
WO	2003-US5043	A2	20030220
WO	2003-US5044	A2	20030220
WO	2003-US5045	A2	20030220
WO	2003-US5162	A2	20030220
WO	2003-US5190	A	20030220
WO	2003-US5234	A2	20030220
WO	2003-US5326	A2	20030220
	2003-US5346	W	20030220
US	2003-417012	<b>A1</b>	20030416
IIS	2003-420194	A2	20030422
WO		<b>A2</b>	20030422
US	2003-422704	A2	20030424
US	2003-424339	A2	20030425
	2003-427160	A2	20030430
US	2003-430882	A2	20030506
US	2003-444853	A	20030523
	2003-US18911		_
		W	20030616
US	2003-607933	A2	20030627
US	2003-485667P	P	20030709
TIC	2003-486729P	P	20030711
US	2003-652791	A2	20030829
US	2003-664767	B2	20030916
	2003-665255	A2	20030916
US	2003-667271	A2	20030916
US	2003-664668	A2	20030918
	2003-665951	A2	20030918
US	2003-670011	A2	20030923
US	2003-683990	A2	20031010
US	2003-512701P	P	20031020
	2003-693059	A2	20031023
US	2003-698311	A2	20031031
US	2003-712633	A2	20031113
	2003-720448		
		A2	20031124
US	2003-724270	<b>A2</b>	20031126
US	2003-726236	<b>A2</b>	20031202
	2003-727780	A2	<u> </u>
			20031203
US	2003-738128	<b>A2</b>	20031218
US	2004-758155	A2	20040112

.

```
US 2004-757803
                      A2
                             20040114
US 2004-764957
                      A2
                             20040126
                             20040210
US 2004-543480P
                      P
US 2004-780447
                      A2
                             20040213
US 2004-783128
                      A2
                             20040220
US 2004-798090
                      A2
                             20040311
US 2004-800487
                      A2
                             20040315
US 2004-824036
                      A2
                             20040414
US 2004-825485
                      A2
                             20040415
US 2004-826966
                      A2
                             20040416
WO 2004-US11848
                      A2
                             20040416
US 2004-830569
                      A2
                             20040423
US 2004-831620
                      A2
                             20040423
WO 2004-US12517
                      A2
                             20040423
US 2004-832522
                      A2
                             20040426
WO 2004-US13456
                      A2
                             20040430
US 2004-570086P
                      P
                             20040511
US 2004-844076
                      A2
                             20040511
                      A2
US 2004-844072
                             20040512
                      A2
WO 2004-US16390
                             20040524
                      A2
US 2004-863973
                             20040609
                      A2
US 2004-864044
                             20040609
US 2004-894475
                      A2
                             20040719
US 2004-922675
                      A2
                             20040820
US 2004-923475
                      A2
                             20040820
US 2004-923536
                      A2
                             20040820
US 2004-944611
                      A2
                             20040916
US 2005-31668
                      A1
                             20050106
US 2005-39680
                      A2
                             20050118
WO 2005-US4270
                      A2
                             20050209
US 2005-98303
                      A2
                             20050404
```

The present invention concerns methods and reagents useful in modulating gene expression in a variety of applications, including use in therapeutic, diagnostic, target validation, and genomic discovery applications. Specifically, the invention relates to small nucleic acid mols., such as short interfering nucleic acid (siNA), short interfering RNA (siRNA), double-stranded RNA (dsRNA), micro-RNA (miRNA), and short hairpin RNA (shRNA) mols. capable of mediating RNA interference (RNAi) against target nucleic acid sequences. Exemplary siNA mols. are synthesized in tandem using standard phosphoramidite synthesis chemical

and a cleavable linker, for example a succinyl-based linker, followed by a one-step purification process that provides RNAi mols. in high yield. Chemical modifications (2'-O-Me and 2'-deoxy-2'-fluoro groups, phosphorothioate linkages, 5'-terminal caps comprising an inverted deoxy abasic moiety, etc.) in siNA constructs are selected to yield nuclease resistance while preserving the ability to mediate RNAi activity. The siNA mols. are designed that can bind to target vascular endothelial growth factor receptor R1 mRNA, hepatitis B virus RNA, and hepatitis C virus RNA, and are optionally individually analyzed by a computer folding algorithm to assess whether the siNA mol. can interact with the target sequence. The siNA mols. are useful in the treatment and diagnosis of prostate cancer and any other condition that responds to modulation of gene expression or activity in a cell, tissue, or organism.

```
L19 ANSWER 5 OF 13 CA COPYRIGHT 2006 ACS on STN
```

AN 138:249768 CA

TI Retroviral expression vectors for efficient transcription of small interfering RNAs in target cells

IN Baltimore, David; Qin, Xiao-Feng; Lois-Caballe, Carlos

PA California Institute of Technology, USA

SO PCT Int. Appl., 56 pp. CODEN: PIXXD2

DT Patent

```
English
LA
FAN.CNT 4
     PATENT NO.
                         KIND
                                 DATE
                                             APPLICATION NO.
                                                                    DATE
                          _ _ _ _
PΙ
     WO 2003023015
                          A2
                                 20030320
                                                                     20020913 <--
                                             WO 2002-US29214
     WO 2003023015
                          A3
                                 20030710
             AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1425400
                          A2
                                 20040609
                                            EP 2002-773370
                                                                     20020912
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     US 2003068821
                          A1
                                 20030410
                                            US 2002-243816
                                                                    20020913 <--
     EP 1424895
                          A2
                                            EP 2002-761659
                                 20040609
                                                                    20020913
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
     JP 2005502355
                          T2
                                 20050127
                                            JP 2003-527080
                                                                    20020913
PRAI US 2001-322031P
                          P
                                20010913
                          P
     US 2002-347782P
                                20020109
                      P
     US 2002-389592P
                                20020618
                          P
     US 2002-406436P
                                20020827
     WO 2002-US29130
                          W
                                 20020912
     WO 2002-US29214
                          W
                                 20020913
     Retroviral expression vectors are described for use in the expression of
AB
     genes for small interfering RNAs in a target cell. Small interfering RNAs
     (siRNAs) that interfere with a viral life cycle by down
     regulating either the viral genome, a viral genome transcript, or an
     essential gene of a host cell may be transcribed from these vectors using
     a promoter for RNA polymerase III. In particular, these constructs can be
     used in the treatment of infection, particularly infection with HIV.
     ANSWER 6 OF 13
                     CA COPYRIGHT 2006 ACS on STN
L19
     138:142441 CA
AN
     Enzymatic nucleic acid peptide conjugates
TI
     Beigelman, Leonid; Azhayev, Alex; Azhayeva, Elena
IN
PA
     Ribozyme Pharmaceuticals, Inc., USA; Antopolsky, Maxim
     PCT Int. Appl., 88 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
FAN.CNT 1
     PATENT NO.
                         KIND
                                DATE
                                            APPLICATION NO.
                                                                    DATE
     WO 2003008628
ΡI
                          A2
                                20030130
                                            WO 2002-US23324
                                                                    20020722 <--
     WO 2003008628
                          A3
                                20031030
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, US, UZ, VN, YU, ZA, ZM, ZW
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
             KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,
             CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                20030807
     US 2003148928
                          A1
                                            US 2002-201389
                                                                    20020722 <--
PRAI US 2001-306995P
                                20010720
                          P
```

- OS MARPAT 138:142441
- AB This invention features conjugates, compns., methods of synthesis, and applications thereof, including galactose, galactosamine, N-acetyl galactosamine, PEG, phospholipid, and human serum albumin (HSA) derived conjugates of nucleosides, nucleotides, non-nucleosides, and nucleic acids including enzymic nucleic acids, DNAzymes, allozymes, antisense, dsRNA, siRNA, triplex oligonucleotides, 2,5-A chimeras, decoys and aptamers.
- L19 ANSWER 7 OF 13 CA COPYRIGHT 2006 ACS on STN
- AN 138:131091 CA
- TI Selective post-transcriptional silencing of oncogene in mammalian cells by siRNA for therapy
- IN Milner, Anne Josephine
- PA UK
- SO PCT Int. Appl., 44 pp.
  - CODEN: PIXXD2
- DT Patent
- LA English
- FAN.CNT 1

	PA	TENT NO	).		KIN	D	DATE	}		APPL	ICAT	ION 1	NO.		D.	ATE	
PI		200300						0130 0717		WO 2	002-	GB33	00		2	0020	717 <
		W: A	E, A	, AL,	AM,	AT,	AU,	AZ,	BA,	BB,	BG,	BR,	BY,	BZ,	CA,	CH,	CN,
•		C	O, CF	, CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		G	M, HF	, HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	KZ,	LC,	LK,	LR,
		I	S, LI	, LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NO,	NZ,	OM,	PH,
		P	L, PI	, RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	TJ,	TM,	TN,	TR,	TT,	TZ,
		U	A, UG	, US,	UZ,	VN,	YU,	ZA,	ZM,	ZW							٠
		RW: G	H, GM	, KE,	LS,	MW,	MZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	AZ,	BY,
		K	G, KZ	, MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		F	I, FR	, GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	SK,	TR,	BF,	ВJ,	CF,
		C	G, CI	, CM,	GA,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG			
	CA	245265	3		AA		2003	0130		CA 2	002-2	2452	653		2	0020	717 <
	EP	143279	_		A2						002-'						
		R: A														MC,	PT,
				, LT,	LV,	FI,	RO,	MK,	CY,	AL,	TR,	BG,	CZ,	EE,	SK		
		200453			T2		2004	1202		JP 2	003-9	51489	90		20	0020	717
		200423			A1		2004	1125		US 2	004-4	4841	01		2	0406	522
PRAI	GB	2001-1	7358		Α		2001	0717									
		2002-6			A		2002	0114									
	GB	2002-1	3855		Α		2002	0617									
	WO	2002-G	B3300		W		2002	0717									

- The present invention relates to a method of selective post-transcriptional silencing in a mammalian cell of the expression of an exogenous gene of viral origin. The method comprises introducing an siRNA construct into a mammalian cell where the siRNA construct is homologous to a part of the mRNA sequence of the exogenous gene. The invention also comprises an siRNA construct with a nucleotide sequence which is homologous to a part of the mRNA sequence of an exogenous gene of viral origin and to the use of such a construct as a medicament. SiRNA causes selective loss of HPV E6 and E7 mRNA. E6 siRNA induces activation of P53 accompanied by p21 expression. E7 silencing results in de-phosphorylation of pRb and induces apoptosis of HPV-positives cells.
- L19 ANSWER 8 OF 13 MEDLINE on STN .
- AN 2003106165 MEDLINE
- DN PubMed ID: 12594334
- TI RNA interference of **influenza** virus production by directly targeting mRNA for degradation and indirectly inhibiting all viral RNA transcription.
- AU Ge Qing; McManus Michael T; Nguyen Tam; Shen Ching-Hung; Sharp

Phillip A; Eisen Herman N; Chen Jianzhu Center for Cancer Research and Department of Biology, Massachusetts CS Institute of Technology, 77 Massachusetts Avenue, Cambridge, MA 02139, USA. NC AI32486 (NIAID) AI40146 (NIAID) AI44477 (NIAID) AI44478 (NIAID) AI50631 (NIAID) CA42063 (NCI) CA60686 (NCI) GM34277 (NIGMS) Proceedings of the National Academy of Sciences of the United States of SO America, (2003 Mar 4) Vol. 100, No. 5, pp. 2718-23. Electronic Publication: 2003-02-19. Journal code: 7505876. ISSN: 0027-8424. CY United States Journal; Article; (JOURNAL ARTICLE)  $\mathtt{DT}$ English LA Priority Journals FS EM 200305 Entered STN: 6 Mar 2003 EDLast Updated on STN: 14 May 2003 Entered Medline: 13 May 2003 Influenza A virus causes widespread infection in the human value. Here we show that short interfering RNAs (siRNAs) influenza virus production in both cell lines and embryonated chicken eggs. The inhibition depends on the presence of a functional antisense strand in the siRNA duplex, suggesting that viral mRNA

AB Influenza A virus causes widespread infection in the human respiratory tract, but existing vaccines and drug therapy are of limited value. Here we show that short interfering RNAs (siRNAs) specific for conserved regions of the viral genome can potently inhibit influenza virus production in both cell lines and embryonated chicken eggs. The inhibition depends on the presence of a functional antisense strand in the siRNA duplex, suggesting that viral mRNA is the target of RNA interference. However, siRNA specific for nucleocapsid (NP) or a component of the RNA transcriptase (PA) abolished the accumulation of not only the corresponding mRNA but also virion RNA and its complementary RNA. These siRNAs also broadly inhibited the accumulation of other viral, but not cellular, RNAs. The findings reveal that newly synthesized NP and PA proteins are required for influenza virus transcription and replication and provide a basis for the development of siRNAs as prophylaxis and therapy for influenza infection in humans.

- L19 ANSWER 9 OF 13 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
- AN 2003:979106 SCISEARCH
- GA The Genuine Article (R) Number: 739WG
- TI Inhibition of virus replication by RNA interference
- AU Haasnoot J; Cupac D; Berkhout B (Reprint)
- Univ Amsterdam, Acad Med Ctr K3110, Dept Human Retrovirol, Meibergdreef 15, NL-1105 AZ Amsterdam, Netherlands (Reprint); Univ Amsterdam, Acad Med Ctr K3110, Dept Human Retrovirol, NL-1105 AZ Amsterdam, Netherlands
- CYA Netherlands
- SO JOURNAL OF BIOMEDICAL SCIENCE, (2003) Vol. 10, No. 6, Part 1, Sp. iss. SI, pp. 607-616.
  ISSN: 1021-7770.
- PB KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND.
- DT General Review; Journal
- LA English
- REC Reference Count: 72
- ED Entered STN: 21 Nov 2003 Last Updated on STN: 21 Nov 2003
  - \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*
- RNA interference (RNAi) is a sequence-specific gene-silencing mechanism in eukaryotes, which is believed to function as a defence against viruses and transposons. Since its discovery, RNAi has been

developed into a widely used technique for generating genetic knock-outs and for studying gene function by reverse genetics. Additionally, inhibition of virus replication by means of induced RNAi has now been reported for numerous viruses, including several important human pathogens such as human immunodeficiency virus type 1, hepatitis C virus, hepatitis B virus, dengue virus, poliovirus and influenza virus A. In this review, we will summarize the current data on RNAi-mediated inhibition of virus replication and discuss the possibilities for the development of RNAi-based antiviral therapeutics. Copyright (C) 2003 National Science Council, ROC and S. Karger AG, Basel.

- L19 ANSWER 10 OF 13 MEDLINE on STN
- AN 2003416308 MEDLINE
- DN PubMed ID: 12954218
- TI The utility of **siRNA** transcripts produced by RNA polymerase i in down regulating viral gene expression and replication of negative- and positive-strand RNA viruses.
- AU McCown Matthew; Diamond Michael S; Pekosz Andrew
- CS Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, MO 63110-1093, USA.
- SO Virology, (2003 Sep 1) Vol. 313, No. 2, pp. 514-24. Journal code: 0110674. ISSN: 0042-6822.
- CY United States
- DT Journal; Article; (JOURNAL ARTICLE)
- LA English
- FS Priority Journals
- EM 200310
- ED Entered STN; 5 Sep 2003 Last Updated on STN: 29 Oct 2003 Entered Medline: 28 Oct 2003
- AB Short interfering double-stranded RNAs (sirNAs) expressed under the control of an RNA polymerase I promoter system were used to target gene expression of influenza A and West Nile virus. Decreased RNA and protein expression was induced in a sequence-specific manner-reducing sequence complementarity from 21 to 17 nucleotides abrogated the sirNA effect. Reduced M(2) expression resulted in a decrease in total and infectious influenza A virus production. WNV protein expression, genomic RNA, and infectious virus production were all dramatically reduced by sirNAs targeting two distinct viral sequences. The data demonstrate the utility of plasmid-driven sirNAs in regulating the expression of single viral genes, global viral gene expression, as a potential antiviral treatment, and as a genetic tool for viruses whose genomes are difficult to manipulate.
- L19 ANSWER 11 OF 13 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
- AN 2003:1044955 SCISEARCH
- GA The Genuine Article (R) Number: 739MR
- TI Improvement of the health status of livestock populations by reproductive-biotechnological technologies
- AU Niemann H (Reprint)
- CS FB Biotechnol, Inst Tierzucht, FAL Mariensee, D-31535 Neustadt, Germany (Reprint); FB Biotechnol, Inst Tierzucht, D-31535 Neustadt, Germany
- CYA Germany
- SO ZUCHTUNGSKUNDE, (SEP-OCT 2003) Vol. 75, No. 5, pp. 401-413. ISSN: 0044-5401.
- PB EUGEN ULMER GMBH CO, POSTFACH 700561 WOLLGRASWEG 41, D-70599 STUTTGART, GERMANY.
- DT Article; Journal
- LA German
- REC Reference Count: 42
- ED Entered STN: 9 Dec 2003
  - Last Updated on STN: 9 Dec 2003
  - \*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS\*

Established reproductive-biotechnological technologies such as ABartificial insemination (AI) and embryo transfer (ET) employing in vivo produced embryos are already valuable tools for the maintenance and improvement of the health status of livestock populations. Transmission of pathogens can be avoided by employing strict hygienic protocols. intact zona pellucida acts as a very efficient barrier against pathogenic infections in in vivo derived embryos. New hygienic challenges arise with the growing use of in vitro produced, cloned and/or transgenic embryos. But the extended experience gained from the global use of in vivo produced embryos forms a solid platform for eventual commercial applications of these types of embryos. However, as the zona pellucida is structurally different or not intact in these embryos major research is needed to ensure that no disease transmission occurs. Further options for the improvement of the health status of livestock populations will evolve from transgenic technologies, in particular when the genome of the major farm animals has been completely sequenced and mapped. Today there are already promising examples for the potential usefulness of this approach to generate disease resistant populations. In the future, gene therapy, DNA vaccination and small interfering RNAs (siRNAs) will also play an important role to maintain and improve the health of farm animals. is predicted that within the next 15-20 years a broad arsenal of technologies based on reproductive biological and molecular genetic tools will become available for improving animal health.

```
L19 ANSWER 12 OF 13 MEDLINE on STN
```

AN 2003546501 MEDLINE

DN PubMed ID: 14625885

TI RNA interference: on the road to an alternate therapeutic strategy!.

AU Dave Rajnish S; Pomerantz Roger J

CS Center for Human Virology and Biodefense, Division of Infectious Diseases and Environmental Medicine, Thomas Jefferson University, Philadelphia, PA 19107, USA.

NC AI43876 (NIAID)

MH58526 (NIMH)

NS27405 (NINDS)

NS44513 (NINDS)

SO Reviews in medical virology, (2003 Nov-Dec) Vol. 13, No. 6, pp. 373-85. Ref: 96

Journal code: 9112448. ISSN: 1052-9276.

CY England: United Kingdom

DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)

LA English

FS Priority Journals

EM 200401

ED Entered STN: 20 Nov 2003 Last Updated on STN: 8 Jan 2004 Entered Medline: 7 Jan 2004

RNA interference (RNAi) is a newly described natural biological phenomenon mediated by small interfering RNA (sirna) molecules which target viral mRNA for degradation by cellular enzymes. RNAi has become a method of choice for studying gene function, especially in mammalian systems. With proof-of-concept studies already presented against a wide variety of human pathogens and several innovative methods of delivering the sirna to a wide variety of primary cells available, the role for sirna as a potential therapeutic strategy is becoming increasingly clear. This review presents recent advances in this direction. Copyright 2003 John Wiley & Sons, Ltd.

L19 ANSWER 13 OF 13 CA COPYRIGHT 2006 ACS on STN

AN 138:14152 CA

TI Preparation of enzymic ribonucleic acid peptide conjugates as antitumor and antiviral agents and compositions for cellular delivery

IN Beigelman, Leonid; Matulic-Adamic, Jasenka; Vargeese, Chandra; Karpeisky,

Alexander; Blatt, Lawrence; Shaffer, Christopher

Ribozyme Pharmaceuticals, Inc, USA PCT Int. Appl., 220 pp. CODEN: PIXXD2 PA

SO

Patent DTLA English

FAN.CNT 235							
PA	PATENT NO.		D DATE	APPLICATION NO.			
PI WO 2002094185		Δ2	20021128	WO 2002-US15876			
				BA, BB, BG, BR, BY,			
				DZ, EC, EE, ES, FI,			
				JP, KE, KG, KP, KR,			
				MK, MN, MW, MX, MZ,			
				SI, SK, SL, TJ, TM,			
			VN, YU, ZA,		111, 111, 12,		
			-	SL, SZ, TZ, UG, ZM,	ZW. AT. BE. CH.		
				GR, IE, IT, LU, MC,			
				GN, GQ, GW, ML, MR,	•		
AU				AU 1998-51819			
		B2					
AU 9939188		. A1		AU 1999-39188	19990713 <		
AU	769175	B2		AU 2000-56616			
EP	1572067	A2		EP 2002-746413			
	R: AT, BE,	CH, DE,	•	GB, GR, IT, LI, LU,			
			FI, RO, MK,				
CA	2447161	AA	20021128	CA 2002-2447161	20020520 <		
JP	2005505504	T2	20050224	JP 2002-590906	20020520		
US	2004110296	A1	20040610	US 2003-427160	20030430		
US	2004192626	A1	20040930	US 2003-444853	20030523		
	2005080031	A1	20050414	US 2003-724270	20031126		
	2004249178	A1	20041209	US 2004-780447	20040213		
US		A1	20050505	US 2004-783128	20040220		
	2005014172	A1	20050120	US 2004-798090	20040311		
US		A1	20050303	US 2004-800487	20040315		
US		A1	20050901	US 2004-824036	20040414		
US	· -	A1	20050310	US 2004-830569	20040423		
US	2005148530 2005233996	A1	20050707	US 2004-831620	20040423		
US 2005137153		A1	20051020	US 2004-832522	20040426		
	2005137133	A1 A1	20050623 20050804	US 2004-840731 US 2004-844076	20040506		
	2005171035	A1	20050721	US 2004-844078	20040511		
US		A1	20050721	US 2004-844072	20040512 20040603		
	2005143333	A1	20050630	US 2004-863973	20040603		
US		A1	20050804	US 2004-864044	20040609		
US		A1	20050602	US 2004-869638	20040609		
US		A1	20050602	US 2004-871222	20040618		
US		A1	20050922	US 2004-877889	20040625		
US	2005124566	A1	20050609	US 2004-879867	20040628		
US	2005130181	A1	20050616	US 2004-881118	20040630		
US	2006142225	A1	20060629	US 2004-881580	20040630		
US	2005124567	A1	20050609	US 2004-883218	20040701		
	2005124568	Al	20050609	US 2004-888226	20040709		
	2005124569	A1	20050609	US 2004-892922	20040716		
US		A1	20050728	US 2004-893010	20040716		
		A1	20050331	US 2004-894475	20040719		
	2005176663	A1	20050811	US 2004-897902	20040723		
		A1	20050908	US 2004-898660	20040723		
		A1	20051215	US 2004-898311	20040723		
US	•	A1	20050818	US 2004-903128	20040730		
		A1	20050721	US 2004-915896	20040811		
	2005159379 2005158735	A1	20050721	US 2004-916030	20040811		
US	2005158735	A1 A1	20050721 20050714	US 2004-916095	20040811		
03	200200012	WT	20050/14	US 2004-918969	20040816		

IIC	2005164966	7.1	20050720	110	2004 010006	20040016
		A1	20050728		2004-918896	20040816
		A1	20050915	US		20040816
US	2005176664	<b>A1</b>	20050811	US	2004-919866	20040817
US	2005176665	A1	20050811	US	2004-919964	20040817
US	2005233997	A1	20051020	US	2004-919584	20040817
	2005136436	A1	20050623	US		20040819
US	2005153915	A1	20050714	US		20040819
US	2005159380	A1	20050721	US	2004-922626	20040819
US	2005159382	<b>A1</b>	20050721	US	2004-923580	20040819
US	2005164967	A1	20050728	US	2004-922034	20040819
	2006142226	A1	20060629			
				US		20040819
	2005079610	A1	20050414	US	2004-923115	20040820
US	2005153916	<b>A</b> 1	20050714	US	2004-923330	20040820
US	2005159381	A1	20050721	US	2004-923522	20040820
US	2005164968	A1	20050728	US	2004-923329	20040820
	2005170371	A1	20050804	US	2004-922340	
						20040820
	2005176666	A1	20050811	US	2004-923182	20040820
US	2005176024	<b>A1</b>	20050811	US	2004-923354	20040820
US	2005176025	<b>A1</b>	20050811	US	2004-923516	20040820
US	2005182007	A1	20050818	US	2004-922675	20040820
	2005182008	A1	20050818	US	2004-923142	
						20040820
	2005182009	A1	20050818	US	2004-923201	20040820
US	2005187174	<b>A1</b>	20050825	US	2004-923181	20040820
US	2005191618	<b>A1</b>	20050901	US	2004-923473	20040820
US	2005196767	A1	20050908	US	2004-923380	20040820
		A1	20051013		2004-923470	20040820
	2005227936	<b>A1</b>	20051013	US	2004-923475	20040820
US	2005233344	<b>A1</b>	20051020	US	2004-923270	20040820
US	2005239731	A1	20051027	US	2004-923379	20040820
US	2005256068	A1	20051117	US	2004-923451	20040820
	2005267058	A1	20051201		2004-922761	
						20040820
	2005288242	<b>A1</b>	20051229		2004-923476	20040820
US	2005209180	<b>A</b> 1	20050922	US	2004-942560	20040915
US	2005233998	<b>A1</b>	20051020	US	2004-944611	20040916
US	2005222066	A1	20051006	US	2004-962898	20041012
	2005261219	A1	20051124		2004-1347	
						20041201
	2005196781	A1	20050908		2004-14373	20041215
	2006019913	A1	20060126	US	2005-31668	20050106
US	2006025361	A1	20060202	US	2005-35813	20050114
US	2005287128	<b>A</b> 1	20051229	US	2005-54047	20050209
US	2005260620	A1	20051124	US	2005-58582	20050215
	2005277133	A1				
			20051215		2005-63415	20050222
	2005282188	A1	20051222	US	2005-98303	20050404
US	2006019917	<b>A</b> 1	20060126	US	2005-140328	20050527
PRAI US	2001-292217P	P	20010518			
US	2001-306883P	P	20010720			
	2001-311865P	P	20010813			
	2002-362016P	P	20020306			
AU	1995-26422	<b>A3</b>	19950518			
US	1996-623891	A	19960325			
AU	1996-76662	<b>A3</b>	19961025			
	2000-181797P	P	20000211			
	2001-780533					
	•	B2	20010209			
	2001-US4273	A2	20010209			
US :	2001-827395	B2	20010405			
US :	2001-294140P	P	20010529			
US :	2001-296249P	P	20010606			
	2001-916466	B1	20010725			
	2001-930423	B2	20010815			
	2001-318471P	P	20010910			
US :	2001-334461P	P	20011130			
US :	2002-35858 <b>0</b> P	P	20020220			
	2002-363124P	P	20020311			
	2002-US9187	A2	20020311			
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		- 1 <u>- 1</u>	20020320			

WO 2002-US10512	A2	20020403	
US 2002-374722P	P	20020422	
US 2002-151116	<b>A</b> 2	20020517	
WO 2002-US15876	W	20020520	
US 2002-157580	<b>A2</b>	20020529	
WO 2002-US16840	<b>A</b> 2	20020529	
WO 2002-US17674			
	A2	20020529	
US 2002-163552	A2	20020606	
US 2002-386782P	P	20020606	
	P	20020703	
US 2002-393924P	P	20020703	
US 2002-396600P	P	20020717	
US 2002-396905P	P	20020718	
US 2002-201394	<b>A2</b>	20020722	
US 2002-398036P	P	20020723	
:			
US 2002-205309	A2	20020725	
US 2002-206705	<b>A2</b>	20020726	
US 2002-399348P	P	20020729	
•			
US 2002-401093P	P	20020805	
US 2002-401104P	P	20020805	
US 2002-404039P	P	20020815	
US 2002-225023	A2	20020821	
US 2002-406784P	P	20020829	
US 2002-408378P	P	20020905	
US 2002-409293P	P	20020909	
US 2002-409493P	P	20020909	
US 2002-238700			
	A2	20020910	
US 2002-409785P	P	20020911	
US 2002-411275P	P	20020917	
<del>-</del>			
US 2002-411707P	P	20020918	
US 2002-251117	A2	20020919	
US 2002-412304P	P	20020920	
US 2002-413714P	P	20020926	
US 2002-418655P	P	20021015	
US 2002-277494	B2	20021021	
US 2002-287949	A2	20021104	
US 2002-425559P	P	20021112	
US 2002-427467P	P	20021119	
US 2002-306747	A2	20021127	
US 2002-429359P	P	20021128	
US 2002-431105P	P	20021205	
US 2003-439922P	P	20030114	
US 2003-440129P	P	20030115	
WO 2003-US2510	A2	20030128	
WO 2003-US3473	A2	20030205	
WO 2003-US3662	$\mathbf{A2}_{\iota_{\perp}}$	20030206	
WO 2003-US4034	A2	20030211	
WO 2003-US4088	A2	20030211	
WO 2003-US4123	A2	20030211	
WO 2003-US4347	A2	20030211	
WO 2003-US4566	A2	20030211	
WO 2003-US7273	<b>A2</b>	20030211	
WO 2003-US4250	A2	20030213	
		<del>-</del> - <del>-</del>	
WO 2003-US4317	A2	20030213	
WO 2003-US4397	A2	20030213	
WO 2003-US4402	A2	20030213	
WO 2003-US4448	A2	20030213	
WO 2003-US4710	A2	20030218	
WO 2003-US4738	A2	20030218	
WO 2003-US4907	A2	20030218	
WO 2003-US4908	A2	20030218	
WO 2003-US4909	A2	20030218	
WO 2003-US4741	<b>A2</b>	20030220	
WO 2003-US4951	A2	20030220	

· WO	2003-US5022	A2	20030220	
	2003 -US5022 2003 -US5028	A2	20030220	
	2003-US5043	A2	20030220	
	2003-US5044	A2	20030220	
WO	2003-US5045	A2	20030220	
WO	2003-US5162	A2	20030220	
	2003-US5190	A	20030220	
	2003-US5234	A2	20030220	
WO	2003-US5326	<b>A2</b>	20030220	
WO	2003-US5346	<b>A2</b>	20030220	
US	2003-417012	A1	20030416	
US	2003-420194	A2	20030422	
	2003-US12626	A2	20030422	
	2003-422704	A2	20030424	
	2003-424339	A2	20030425	
, US	2003-427160	A2	20030430	
US	2003-430882	A2	20030506	
US	2003-444853	A2	20030523	
	2003-607933	A2	20030627	
	2003-486729P	P	20030711	
US	2003-652791	A2	20030829	
US	2003-664767	B2	20030916	
US	2003-665255	A2	20030916	
US	2003-667271	A2	20030916	
	2003 -664668	A2		
			20030918	
	2003-665951	A2	20030918	•
	2003-670011	A2	20030923	
US	2003-683990	A2	20031010	
US	2003-512701P	P	20031020	
	2003-693059	A2	20031023	
	2003-698311	A2		
			20031031	
	2003-712633	A2	20031113	
US	2003-720448	A2	20031124	
US	2003-724270	A2	20031126	
US	2003-726236	A2	20031202	
	2003-727780	A2	20031202	
	2003-738128	A2	20031218	
	2004-758155	A2	20040112	
US	2004-757803	A2	20040114	
US	2004-764957	A2	20040126	
	2004-543480P	P	20040210	
	2004 3434801			
		A2	20040213	
	2004-783128	A2	20040220	
US	2004-798090	A2	20040311	
US	2004-800487	A2	20040315	
	2004-824036	A2	20040414	
	2004 -825485			
		A2	20040415	
	2004-826966	A2	20040416	
WO	2004-US11848	A2	20040416	
US	2004-830569	A2	20040423	
	2004-831620	A2	20040423	
	2004-US12517	A2	20040423	
	2004-832522	A2	20040426	
WO	2004-US13456	A2	20040430	
US	2004-570086P	P	20040511	
US	2004-844076	A2	20040511	
	2004-844072	A2	20040511	
	2004-US16390	A2	20040524	
	2004-863973	A2	20040609	
US	2004-864044	A2	20040609	
US	2004-894475	A2	20040719	
	2004-922675	A2	20040820	
	2004 922675			
ווכ	ムロロマーフムラサ / コ	A2	20040820	
	2004-923536	A2	20040820	

.

US	2004-944611	A2	20040916
US	2005-31668	A1	20050106
US	2005-39680	A2	20050118
WO	2005-US4270	A2	20050209
US	2005-98303	A2	20050404

GI

AB This invention features peptide nucleotide conjugates I wherein each R1-R8 are independently hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, or a protecting group, each "n" is independently an integer from 0 to about 200, R9 is a straight or branched chain alkyl, substituted alkyl, aryl, or substituted aryl, and R2 is a phosphorus containing group, nucleoside, nucleotide, small mol., nucleic acid, or a solid support comprising a linker., degradable linkers, compns., methods of synthesis, and applications thereof, including folate, galactose, galactosamine, N-acetyl galactosamine, PEG, phospholipid, peptide and human serum albumin (HAS) derived conjugates of biol. active compds., including antibodies, antivirals, chemotherapeutics, peptides, proteins, hormones nucleosides, nucleotides, non-nucleosides, and nucleic acids including enzymic nucleic acids, DNAzymes, allozymes, antisense, dsRNA, siRNA, triplex oligonucleotides, 2,5-A chimeras, decoys and aptamers. 1-O-(4-monomethoxytrityl)-N-(12'-hydroxydodecanoyl-2-acetamido-3,4,6-tri-Oacetyl-2-deoxy-3-D-galactopyranose)-D-threoninol 3-0-(2-cyanoethyl,N,Ndiisopropylphosphorami-dite) was prepared and incorporated into RNA. A method of treating a cancer patient, comprising contacting cells of patient wherein said cancer is breast cancer, lung cancer, colorectal cancer, brain cancer, esophageal cancer, stomach cancer, bladder cancer, pancreatic cancer, cervical cancer, head and neck cancer, ovarian cancer, melanoma, lymphoma, glioma, or multidrug resistant cancers and/or viral infections including HIV, HBV, HCV, CMV, RSV, HSV, poliovirus, influenza, rhinovirus, west nile virus, Ebola virus, foot and mouth virus, and papilloma.

Ι